Claims

1. (Previously presented) A method of producing a protein with an increased antimicrobial activity or polypeptide stability, comprising:

replacing an arginine residue in a polypeptide of interest with a tryptophan residue or a phenylalanine residue to produce a tryptophan-substituted or phenylalanine-substituted polypeptide; and

comparing the antimicrobial activity or polypeptide stability of the polypeptide of interest with the tryptophan-substituted or phenylalanine-substituted polypeptide, wherein the tryptophan-substituted or phenylalanine-substituted polypeptide has increased antimicrobial activity or polypeptide stability compared to the polypeptide of interest, and wherein the tryptophan-substituted or phenylalanine-substituted polypeptide has similar antimicrobial activity or increased polypeptide stability compared to the polypeptide of interest wherein the arginine residue is ADP-ribosylated, thereby producing the protein with increased antimicrobial activity or polypeptide stability.

2. (Previously presented) The method of claim 1, wherein the tryptophan-substituted or phenylalanine-substituted polypeptide has an increased antimicrobial activity.

3. (Original) The method of claim 2, wherein the antimicrobial activity comprises chemotaxis of T cells, neutrophil recruitment, or cytokine release.

4. (Original) The method of claim 3, wherein the cytokine release comprises interleukin-8 release.

5. (Original) The method of claim 2, wherein the protein is a defensin.

6. (Original) The method of claim 5, wherein the defensin is an alpha defensin.

7. (Previously presented) The method of claim 2, wherein the arginine residue is substituted with a tryptophan residue.

8. (Previously presented) The method of claim 2, wherein the arginine residue is substituted with a phenylalanine residue.

9. (Previously presented) The method of claim 2, wherein the activity is increased as compared to the polypeptide of interest.

10. (Previously presented) The method of claim 2, wherein the stability is increased as compared to the polypeptide of interest.

11. (Previously presented) The method of claim 2, wherein the increased activity or stability is a 100% increase, as compared to a control polypeptide.

12. (Previously presented) The method of claim 2, wherein the increased activity or stability is a 50% increase, as compared to a control polypeptide.

13-28. (Canceled)

29. (Previously presented) A method of increasing antimicrobial activity or polypeptide stability of a defensin polypeptide of interest, comprising:

substituting an arginine residue in the defensin polypeptide of interest with a tryptophan or a phenylalanine to produce a tryptophan-substituted or phenylalanine-substituted defensin polypeptide;

comparing the antimicrobial activity or polypeptide stability of the defensin polypeptide of interest with the tryptophan-substituted or phenylalanine-substituted defensin polypeptide, wherein the tryptophan-substituted or phenylalanine-substituted defensin polypeptide has increased antimicrobial activity or polypeptide stability compared to the defensin polypeptide of interest, and wherein the tryptophan-substituted or phenylalanine-substituted defensin polypeptide has similar antimicrobial activity or increased polypeptide stability compared to the defensin polypeptide of interest wherein the arginine residue is ADP-ribosylated,

thereby increasing the antimicrobial activity or the polypeptide stability of the defensin polypeptide.

30. (Original) The method of claim 29, wherein the defensin polypeptide is an alpha defensin.

31. (Canceled)

32. (Previously presented) The method of claim 29, wherein the antimicrobial activity comprises T cell chemotaxis, neutrophil recruitment, or cytokine release.

33. (Previously presented) A method of increasing an antimicrobial immune response in a subject infected with or at risk of being infected with a microbe, comprising administering to the subject a therapeutically effective amount of a defensin polypeptide comprising an amino acid substitution, wherein the amino acid substitution is a replacement of an arginine in a defensin polypeptide of interest with a tryptophan or a phenylalanine to produce a tryptophan-substituted or phenylalanine-substituted defensin polypeptide, wherein the tryptophan-substituted or phenylalanine-substituted defensin polypeptide has similar antimicrobial activity or increased polypeptide stability, compared to the defensin polypeptide of interest wherein the at least one arginine residue is ADP-ribosylated,
thereby increasing the antimicrobial immune response in the subject infected with or at risk of being infected with a microbe.

34. (Original) The method of claim 33, wherein the immune response comprises T cell chemotaxis, neutrophil recruitment, or cytokine release.

35. (Original) The method of claim 33, wherein the subject has an immune disorder.

36-48. (Canceled)